

REMARKS

Claims 1-4, 7-16, 19-31, 33-37 and 39 are pending. Claims 1-4, 7-16, 19-31, 33-37 and 39 are rejected under the judicially created doctrine of obviousness-type double patenting and under 35 U.S.C. § 103(a) for being allegedly obvious over cited references. For reasons set forth herein, the rejections should be removed and the claims should be deemed allowable.

As a preliminary matter Applicant's note that the Domestic Priority data as claimed has been cited incompletely on the Official Filing Receipt mailed March 24, 2004. The correct priority claim was filed along with the application on July 30, 2003 in a preliminary amendment under 37 C.F.R. § 1.78(a)(2)(i). This document was properly received and made of record in the present application as evidenced by its presence in the image file wrapper of the instant application on the Patent Application Information Retrieval system. A copy of the filed preliminary amendment is provided herewith along with a redlined copy containing the corrected priority claim. Applicants hereby respectfully request the issuance of a corrected Official Filing Receipt.

The Double Patenting Rejection Should Be Withdrawn:

Claims 1-4, 7-16, 19-31, 33-37, and 39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,582,719 or claims 1-55 of U.S. Patent No. 6,106,505, each in view of International Patent Publication No. WO 97/25085, U.S. Patent No. 5,624,704, U.S. Patent No. 5,688,516 and Domenico et al., (Journal of Antimicrobial Chemotherapy, 28(6):801-810, 1991).

The Examiner has indicated that the conflicting claims are not identical.

According to the Examiner, claims 1-15 of U.S. Patent No. 6,582,719 do not expressly claim the use of bismuth citrate bismuth salicylate, chlorhexidine gluconate, triclosan or a zinc salt, and claims 1-55 of U.S. Patent No. 6,106,505 do not expressly claim the use of minocycline, bismuth citrate or bismuth salicylate, chlorhexidine gluconate, benzalkonium chloride or a zinc salt. However, according to the Examiner, the claimed invention, as a whole, would have been an obvious modification of the claims of U.S. Patent No. 6,582,719 or U.S. Patent No. 6,106,505 to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of said claims and the cited secondary references.

Applicants note that U.S. Patent No. 6,106,505 ('505 patent) is directed to the treatment of polymeric medical articles utilizing specific combinations of chlorhexidine and triclosan, both antiseptic agents. The '505 patent does not claim combining an antibiotic and antiseptic agent to treat a polymeric medical article. Even in view of the additional references cited by the Examiner, Applicants do not agree that an obviousness-type double patenting rejection applies. Both antiseptics and antibiotics are comprised of a large group of members. Combining the disclosure of the '505 patent with the cited references does not collectively teach an effective combination even to a skilled artisan since a large number of possible combinations and dosages exists. Accordingly, the rejection as regards the '505 patent should be withdrawn.

As regards United States Patent No. 5,582,719, Applicants will submit a terminal disclaimer upon notification of allowance of allowable subject matter.

The Rejections Under 35 U.S.C. § 103(a) Should Be Withdrawn:

Claims 1-4,7-16, 19-3 1,33-37,39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Raad et al. (United States Patent No. 5,688,516) in view of Darouische et al. (United States Patent No. 6,719,991 or United States Patent No. 5,624,704), WO 97/25085 and Domenico et al. (Journal of Antimicrobial Chemotherapy, 28(6):801-810,1991).

The Examiner states:

The difference between the claimed invention and the prior art is that the prior art does not expressly disclose the combination of minocycline and chlorohexidine, the combination of minocycline, triclosan and bismuth, or minocycline and bismuth for treating a polymeric-containing medical articlet. However, the prior art amply suggest the same as the prior art discloses that chlorohexidine, such as chlorohexidine digluconate, can be combined with triclosan, that minocycline can be combined with chelating agents such as zinc citrate and citrate and bismuth, that bismuth nitrate and bismuth subsalicylate are effective in inhibiting the formation of capsular polysaccharide by bacteria which forms bacterial biofilm, that minocycline can be combined with triclosan or chlorohexidine and that chlorohexidine can be combined with triclosan, silver sulfadiazine or benzalkonium chloride. As such, it would have been well within the skill of to modify the prior art as above with the expectation that any chlorohexidine salt, including chlorohexidine gluconate in combination with triclosan would be suitable for coating a catheter, that zinc cirate or citrate and bismuth in combination with minocycline would be effective in killing bacteria on catheters and inhibiting the formation of glycocalyx, that bismuth salicylate or bismuth citrate could be used instead of bismuth nitrate or in combination with bismuth nitrate to inhibit the formation of glycocalyx or biofilm, that silver sulfadiazine or benzalkonium chloride can be combined with chlorohexidine and triclosan for treating catheters and that minocycline can be combined with chlorohexidine and triclosan for treating catheters.

Applicants respectfully disagree. To establish a prima facie case of obviousness, three basic criteria must be met (MPEP 2142). First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally

available to one of ordinary skill in the art to modify the reference or to combine the teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on Applicant's disclosure. *In re Vaeck* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1981). Thus, the prior art reference(s) must teach or suggest all the claim limitations. Both the suggestion and a reasonable expectation of success must be present in the references themselves.

The Cited Art Does Not Provide a Reasonable Expectation Of Success Nor Teach Or Suggest All Claim Limitations

The Examiner has stated that U.S. Patent No. 5,688,516 ('516 patent) discloses: (i) chelating agents preventing adherence to surfaces by inhibiting formation of a glycocalyx; and (ii) a tetracycline antibiotic such as minocycline when combined with a chelating agent is effective in killing adherent microorganisms. The Examiner has cited various sections of the '516 patent e.g. column 1, lines 60-68, column 2, lines 1-11, claims 1, 2, 9, 10, 11, 14-17 etc., to support the rejection. Applicants note that the cited sections of the '516 patent pertaining to (i) and (ii) above, merely disclose the already well known role of a glycocalyx in adherence (column 2), a list of possible chelating agents (column 4), and the general possibility of combining minocycline with either a chelating agent, anticoagulant or antithrombic agent (column 6). In addition, claims for the '516 patent have been reissued to limit the invention (claim 1) to a combination of a non-glycopeptide antimicrobial agent from a large possible list of alternatives (claims 8-12), a chelating agent and a second agent selected from an anticoagulant or antithrombic agent. Thus, the cited reference provides no

teachings to indicate that a combination of a specific antiseptic agent combined with a specific tetracycline antibiotic will be effective in producing an anti-infective medical article of the present invention. Nor does the cited reference provide any teachings to indicate what specific concentration range of agents used in a specified combination will be effective. In addition, the cited reference appears to suggest that additional anticoagulant or antithrombic agents may be required.

If the teachings of the '516 patent were combined with U.S. Patent No. 6,719,991 ('991 patent) or U.S. Patent No. 5,624,704 ('704 patent) the deficiency noted above is not removed. The '991 patent at the sections cited by the Examiner again merely lists several antimicrobial or antiseptic agents without disclosing which if any may be used in an effective combination and at what specific concentration. The '991 patent in addition is directed to the use of a combination of an antimicrobial agent together with a non-pathogenic bacterial agent, said composition being applied to a surface of a medical device.

WO 97/25085 suffers from a similar deficiency. Pages 5 and 6 cited by the Examiner against the present application merely disclose a long list of chlorhexidine derivatives or medical devices respectively. Page 14, lines 3-9 of the reference discloses a list of possible anti-infective agents without any teachings of dosage or effective combinations. Similarly, there is no disclosure provided in Domenico et al. to apprise one of skill in the art of the need to combine a bismuth salt at a specified concentration so as to be effective in combination with the other agents utilized by the instant invention, to produce an anti-infective medical article.

Applicants note that the present invention provides: (i) several working examples which determine and demonstrate not only effective working

combinations of an antiseptic and antibiotic, but also that many combinations are ineffective under identical test conditions. For example Table XII at page 26 discloses a specific combination, demonstrating broad spectrum antimicrobial activity against the most frequent medical device contaminating organisms. Several other working examples disclosed in the instant application shows that a specific effective combination of two or more agents cannot be merely obtained by combining information from the prior art. Thus, for the above reasons, the combination of the cited references does not render the claimed invention obvious. It is therefore requested that the rejection be removed.

Applicants do not believe that any additional fee is required in connection with the submission of this document. Should any additional fees be required, the Commissioner is hereby authorized to charge any additional fees to Deposit Account 02-4377. A duplicate copy of this communication is provided.

Respectfully submitted,

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